UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: February 10, 2011

SUBJECT: Chemistry and Toxicology Scoping Document for the Registration Review of 2-Phenethyl Propionate.

Registration Review Case #:	3110
PC Code:	102601
CAS #:	122-70-3
Chemical Class:	Biochemical

FROM: Angela L. Gonzales, Biologist 02/10/11
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Biopesticides & Pollution Prevention Division (7511P)

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ACTION REQUESTED

The following scoping document contains the preliminary chemistry and human health assessment for the biopesticide 2-phenethyl propionate (2-PEP) in support of the development of the Registration Review Work Plan.

Executive Summary

Based on the available data and information, the Agency does foresee the need for new data and risk assessments for 2-PEP. All product chemistry data requirements per 40 CFR 158.2030 have been satisfied. All human health assessment data requirements per 40 CFR 158.2050 have been fulfilled with the exception of the acute inhalation, 90-day dermal, 90-day inhalation, mutagenicity and developmental toxicity data requirements. Data and or information must be submitted in order to complete the toxicology database for this active ingredient and to establish the potential for toxicity to humans. The need for these data is based primarily upon the following: 1) according to the Incident Data System, there have been 421 reports of incidents (312 human incidents) from use of products containing this chemical as an active ingredient; 2) the potential for exposure exists from use of products containing the 2-PEP (particularly for the dermal and inhalation routes of exposure); 3) a risk assessment cannot be completed without fulfillment of the identified data gaps in the toxicology database.

I. Background

2-PEP is the ester of phenethyl alcohol and propionic acid. It is a component of peppermint oil (*Mentha piperita, L*) (Dayan, 2009). The active ingredient is employed as an attractant in Japanese and Oriental beetle traps and baits and is also used as an insecticide.

The ingredient was first registered by the Agency in June, 1983. There are currently 13 end-use products (EPs) containing the active ingredient that are registered. Twelve of these products contain other active ingredients; only one product contains 2-PEP as the sole active ingredient. There are no manufacturing-use products (MPs) registered by the Agency at this time.

2-Phenethyl propionate is classified as a minimum risk pesticide that is exempt from the requirements of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) under 40 CFR 125.25(f) when all criteria under this exemption are met. The ingredient is approved by the Food and Drug Administration (FDA) as a synthetic flavoring substance and adjuvant for direct addition to food under 21 CFR 172.515. It is currently not approved for use as an inert ingredient in pesticide products.

II. Tolerance

There are no tolerances or tolerance exemptions for this active ingredient.

III. Incidents

According to the Incident Data System, there have been 421 incidents reported between January 1, 1992 and October 2, 2009 for products containing 2-PEP as an active ingredient. All of the products contain 2-PEP in addition to one or more other active ingredients. Of the 421 incidents, 312 are considered to be minor human incidents, 1 is a human incident with symptoms unknown,

and 108 are domestic animal incidents. Incidents have been reported from use of traps, impregnated baits, dust and spray formulations and pressurized liquid formulations. It is not clear from the data available to the Agency how many of these incidents were the result of misuse of products. The following symptoms were the most commonly reported in the human incident data: respiratory irritation, dermal irritation, eye irritation, vomiting, hives, and rashes. Other symptoms included dizziness, seizures, fever, and chest pain, among others.

IV. Active Ingredient Characterization

All of the required product chemistry data requirements have been satisfied on the active ingredient. The product chemistry data submitted are summarized in Table 1 and the physical and chemical properties data are summarized in Table 2.

TABLE 1. Product Chemistry Data Requirements for *2-Phenethyl Propionate* (40 CFR § 158.2030)

OCSPP Guideline No.	Study	Results	MRID
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Data requirements have been satisfied. Data are required for unregistered sources of the active ingredient.	41614401 43029001
830.1700	Analysis of samples	Data requirement has been satisfied. Data are required for unregistered sources of the active ingredient.	
830.1750	Certification of limits	Data requirement has been satisfied. Data are required for unregistered sources of the active ingredient.	
830.1800	Analytical method	Data requirement has been satisfied. Data are required for unregistered sources of the active ingredient.	

TABLE 2. Physical and Chemical Properties of *2-Phenethyl Propionate* (40 CFR § 158.2030)			
OCSPP Guideline No.	**Property**	**Description of Result**	**MRID**
830.6302	Color	Colorless to pale yellow	42262902 47255021
830.6303	Physical State	Liquid	47255021
830.6304	Odor	Herbaceous-rosy, deep fruity, slightly spicy	47255020 and 47255021
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Stable for 24 months in a tightly closed container in a cool, dry place protected from heat and light.	47255021
830.6315	Flammability	Flash point > 200 °F (closed cup) Flash point >212.00 °F (> 100.00°C)	47255020 47255021
830.6317	Storage Stability	Not required for TGAI	
830.6319	Miscibility	Not required for TGAI	
830.6320	Corrosion Characteristics	Not required for TGAI	
830.7000	pH	5.74 6.2 ± 0.2 at 20°C (1% w/v solution)	42262902 47648404
830.7050	UV/Visible Light Absorption	ε, L/(cm-mol) = 244 (neutral conditions) ε, L/(cm-mol) = 245 (acidic conditions) ε, L/(cm-mol) = 259 (basic conditions)	47553704
830.7100	Viscosity	Not required for TGAI	
830.7200	Melting Point/Range	Not required; 2-PEP is not a solid at room temperature	
830.7220	Boiling Point/Range	248 °C 238°C	42262902 47648401
830.7300	Density	1.01 g/ml at 25°C 1.00900 to 1.01700 g/cm^3 at 25°C	47255020 47255021
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not required at this time.	
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Log K_{ow} = 3.06 (estimated)	47255023
830.7840	Water Solubility	84.014 mg/L at 25°C (estimated) 278 mg/L at 25°C (estimated)	47648401 HSDB, 2010

TABLE 2. Physical and Chemical Properties of *2-Phenethyl Propionate* (40 CFR § 158.2030)			
OCSPP Guideline No.	**Property**	**Description of Result**	**MRID**
830.7950	Vapor Pressure	10 mmHg at 25°C	42262902
		0.0514 mmHg (estimated)	47255022

V. Toxicity Profile

Data gaps have been identified regarding the toxicity data requirements for this active ingredient and are discussed below. The data available to the Agency are summarized in Table 3 below.

Table 3. Human Health Assessment Data Requirements for *2-Phenethyl Propionate* (40 CFR § 158.2050)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	LD_{50} = 4,500 mg/kg (3,590 - 5,640 mg/kg) in males; 4,400 mg/kg (4,780 – 4,050 mg/kg) in females LD_{50} = 4,000 mg/kg	III	42262903 HSDB, 2010
Acute dermal toxicity (rabbit) (870.1200)	LD_{50} > 2,000 mg/kg (single dose tested) LD_{50} > 5,000 mg/kg	IV	42262904 HSDB, 2010
Acute inhalation toxicity (rat) (870.1300)	**Data gap: based on potential for exposure and the available incident data it cannot be determined if exposure to 2-PEP would result in toxicological effects.**		
Primary eye irritation (rabbit) (870.2400)	All irritation cleared by 72 hours; minimally irritating.	III	42262905
Primary dermal irritation (rabbit) (870.2500)	Mild irritation at 72 hours; moderately irritating based on primary dermal irritation index.	IV	42262906
Dermal sensitization (Buehler-guinea pig) (870.2600)	Not a sensitizer		42262907
Hypersensitivity incidents (885.3400)	Must be reported as adverse effects data.		
90-Day oral toxicity (870.3100)	Not required based on current use patterns; no uses on food. Non-food uses are not likely to result in repeated oral exposure to humans.		
90-Day dermal toxicity (870.3250)	**Data gap: based on potential for exposure and the available incident data it cannot be determined if exposure to 2-PEP would result in toxicological effects.**		
90-Day inhalation toxicity (870.3465)	**Data gap: based on potential for exposure and the available incident data it cannot be determined if exposure to 2-PEP would result in toxicological effects.**		
Mutagenicity (870.5100, 5300 and 5375)	**Data gap: based on potential for exposure and the available incident data it cannot be determined if exposure to 2-PEP would result in toxicological effects.**		
Developmental toxicity (870.3700)	**Data gap: based on potential for exposure and the available incident data it cannot be determined if exposure to 2-PEP would result in toxicological effects.**		

Data gaps in Table 3 above are identified based on the lack of toxicology data and information available to the Agency to satisfy these requirements, use patterns of products containing this active ingredient that are likely to result in human exposure (particularly inhalation, although the potential for dermal exposure also exists), and incident data that have been submitted to the Agency. Although the reported incidents are from use of products containing 2-PEP and other active ingredients, it cannot be determined based on the information available to the Agency which entity (or entities) is responsible for the deleterious human effects.

VI. References

Dayan FE, Cantrell CL and Duke SO. "Natural Products in Crop Protection". 2009. *Bioorganic and Medicinal Chemistry*. 17(12): 4022-4034. <http://etmd.nal.usda.gov/bitstream/10113/36220/1/IND44288781.pdf>

Hazardous Substances Data Bank (HSDB). "2-Phenethyl Propionate". 2006. National Library of Medicine. 29 December 2010. < http://www.toxnet.nlm.nih.gov/cgi-bin/sis/search>

cc: A. L. Gonzales, C. Greene, BPPD Science Review File, IHAD/ARS
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